REMARKS

Claims 37-44 were pending in the subject application. Applicants have canceled claims 38, 40 and 44 without prejudice to Applicant's right to prosecute claims of similar or differing scope in subsequent applications. Claims 37, 39, 41 and 42 have been amended to more clearly describe the claimed invention. Applicants have added claims 45-47. Applicants respectfully request entry of the amendment such that claims 37, 39, 41-43 and 45-47 will be pending.

Restriction

Applicants acknowledge that the Examiner has made the restriction requirement final to which Applicants had elected an invention with traverse.

Specification

The Office Action objects to the abstract because it contains more than 150 words. The Office Action requests correction and further requests that the abstract be amended to "more fully describe the embodiments of the invention now being described *i.e.* methods of inhibiting transcription and/or translation of mammalian CDC25A genes." In response, Applicants have amended the abstract to reduce its length and to recite an embodiment of the invention being claimed. Applicants request reconsideration and withdrawal of this ground of rejection.

Claim rejections 35 USC 112 2nd Paragraph

The Office Action rejects claims 37-44 as allegedly failing to particularly point out and distinctly claim the subject matter which Applicants regard as their invention. Specifically, the Office Action alleges that the phrase "an oligonucleotide that hybridizes to a sequence encoding a mammalian CDC25A protein, or the complement of said sequence, under stringent conditions of 5-10 °C below the calculated melting temperature T_m of said sequence" is unclear. In response, without conceding the correctness of the Examiner's argument but merely to expedite allowance of the claims, Applicants have amended claim 37 to clarify the subject matter.

Claim Rejections 35 USC 112 1st Paragraph (Written Description)

Claims 37-44 are rejected under 35 USC 112 1st paragraph as allegedly failing to comply with the written description requirement. The Office Action alleges that the claimed method

encompasses inhibition of gene expression in many different mammals and each mammal may be treated by many different oligonucleotides capable of hybridizing to the target gene, and that the specification does not provide written description to support the broad genus of oligonucleotides and mammals encompassed by the claims. The Office Action further alleges that the description fails to describe both how to perform the claimed method and specific structures capable of inhibiting expression of CDC25A or variants thereof.

In response, Applicants traverse the Examiner's rejection. Nevertheless, without conceding the correctness of the Examiner's argument, Applicants have amended claim 37 to clarify the features of the oligonucleotide. As amended, claim 37 does not recite the use of just any oligonucleotide (as the Office Action had characterized claim 37 prior to the current amendment), but rather the use of only those oligonucleotides that hybridize to a nucleic acid consisting of the sequence set forth in SEQ ID NO:1. Applicants have further amended the claim 37 to recite "human CDC25A" rather than "mammalian cdc25A". Applicants note that they have also added claim 45, which refers to the use of oligonucleotides that (i) are complementary to the sequence set forth in SEQ ID NO: 1 or to a portion thereof; and (ii) hybridize to the polynucleotide or to its complement.

Oligonucleotides

The structure and the function of the oligonucleotides provide an adequate description of the genus of oligonucleotides that may be used in the claimed methods, including common structural features relative to SEQ ID NO:1, and therefore satisfy the written description requirement.

This assertion is supported by the Federal Circuit's finding in The Regents of the University of California v. Eli Lilly and Co., 119 F.3d 1559, 1997 U.S. App. LEXIS 18221, 43 U.S.P.Q.2D (BNA) 1398 (Fed. Cir. 1997). The Federal Circuit addressed the question of how to adequately describe a genus of materials. In outlining that which constitutes an adequate description of a genus with respect to genetic material, the court asserted that adequate description requires more than the gene or protein name.

> "[A] cDNA is not defined or described by the mere name "cDNA," even if accompanied by the name of the protein that it encodes, but

> requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the DNA. See Fiers, 984 F.2d at 1171, 25 U.S.P.Q.2D (BNA) at 1606. A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus **or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus."** (emphasis supplied) 119 F.3d at 1566

Accordingly, for the description of a genetic invention to be deemed adequate to describe the genus that the claims encompass requires either a recitation of the structure (i.e., sequence) of a representative number of members of the genus **or** a recitation of the common features of the members of the claimed genus. This "recitation of structural features common to the members of the genus" is analogous to the way in which chemical genera are described, and provides features which readily allow one of skill in the art to recognize the claimed invention. This is in contrast to the way in which the claimed subject matter was recited in Lilly, where nucleic acids were claimed by the name of the cDNA and its origin, without any recitation of sequence or common structural or functional characteristics that could be used by one of skill in the art to readily envision the claimed sequences.

> "In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus." 119 F.3d at 1566

Applicants submit that the pending claims define the oligonucleotide in terms of generic formulae that indicate with specificity what sequences the claims encompass, and accordingly meet the guidelines set forth above and comply with the written description requirement.

Target CDC25A

The Office Action alleged that the claims failed to comply with the restriction requirement, in part, because claim 37 was drawn "to method of inhibiting transcription or translation of a polynucleotide encoding mammalian CDC25A protein, [yet] only the human CDC25A protein and the gene encoding it (SED ID NOS:2 and 1, respectively) have been described in the specification." In response and as noted above, claims 37 has been amended so that it recites "human CDC25A" rather than "mammalian CDC25A," thereby obviating this ground of rejection.

Examples of Performing Claimed Method

The Office Action asserts that the specification fails to provide working examples or a description of how to perform the claim method *i.e.* how to perform antisense inhibition. Applicants submit that to satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116.

At the time the subject application was filed, it was well-known that the transcription and translation of a target gene could be inhibited using an antisense oligonucleotide directed to the target gene. For example, the following U.S. Patents granted prior to the filing of the subject application describe antisense oligonucleotides to target genes: 5,271,941: "Antisense oligonucleotides of human regulatory subunit RIα of cAMP-dependent protein kinases"; 5,098,890: "Antisense oligonucleotides to c-myb proto-oncogene and uses thereof"; 5,256,648: "Selective inhibition of gene expression by photoactivatable oligonucleotides"; 5,248,670: "Antisense oligonucleotides for inhibiting herpes viruses"; 4,806,463: "Inhibition of HTLV-III by exogenous oligonucleotides"; 5,135,917: "Interleukin receptor expression inhibiting antisense oligonucleotides"; 5,268,295: "Mammalian adipocyte protein p154, nucleic acids coding therefor and uses thereof.".

MPEP 2163(II)(A)(3)(a) states that what is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. See *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d at 1384, 231 USPQ at 94." Therefore, since performing antisense

inhibition of a target gene of known sequence was conventional and well-known to one of ordinary skill in the art, the instant specification need not describe in detail how to perform antisense inhibition to comply with the written description requirement. The instant specification describes the sequence of human CDC25A in detail, which together with the knowledge in the art for performing antisense inhibition is sufficient to comply with the written description requirement.

In light of the arguments set forth above and the amendment to claim 37, Applicants respectfully request reconsideration and withdrawal of the written description rejection. Nevertheless, in the event that the written description rejection is maintained in a subsequent Office Action, Applicants respectfully remind the examiner that pursuant to MPEP 2163.04(II), before repeating any rejection under 35 U.S.C. **http://www.uspto.gov/web/offices/pac/mpep/documents/appxl_35_U_S_C_112.htm - usc35s112**112, 1st paragraph, for lack of written description, the Examiner must (i) review the basis for the rejection in view of the record as a whole, including amendments to claim 37 and new claims 45-47, arguments and evidence submitted by applicant, (ii) fully respond to applicant's rebuttal arguments, and (iii) properly treat any further showings submitted by applicant in the reply.

Claim Rejections 35 USC 112 1st Paragraph (Enablement)

Claims 37-44 are rejected under 35 USC 112 1st paragraph as allegedly failing to comply with the enablement requirement. While conceding that the specification is enabling for performing the claimed method *in vitro*, the Office Action alleges that the specification does not enable performing the method *in vivo*. Without conceding the correctness of the Examiner's argument but merely to expedite allowance of the claims, Applicants have amended claim 37, from which all other claims depend, to recite "in a cell *in vitro*", thereby excluding embodiments wherein the method is performed *in vivo* in a mammal. Accordingly, Applicants request reconsideration and withdrawal of this ground of rejection.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 18-1945, under Order No. GPCI-P10-019 from which the undersigned is authorized to draw.

Dated: Thursday, December 23, 2004

Respectfully submitted,

By _____

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